

=> d his

(FILE 'HOME' ENTERED AT 12:23:14 ON 14 AUG 2006)

FILE 'REGISTRY' ENTERED AT 12:23:28 ON 14 AUG 2006

L1 STRUCTURE UPLOADED

L2 STRUCTURE UPLOADED

L3 1 S L1 OR L2

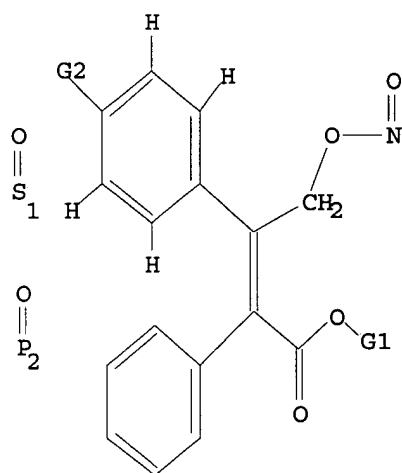
L4 22 S L3 FULL

FILE 'CAPLUS' ENTERED AT 12:24:52 ON 14 AUG 2006

L5 2 S L4

=> d que l5 stat

L1 STR

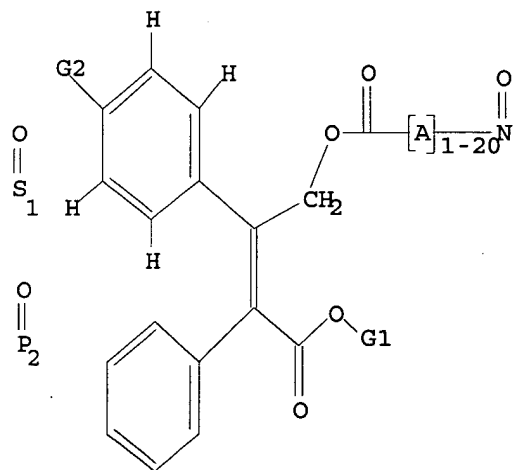


G1 H, Cy, Ak

G2 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

L2 STR



G1 H, Cy, Ak

G2 [@1], [@2]

Structure attributes must be viewed using STN Express query preparation.

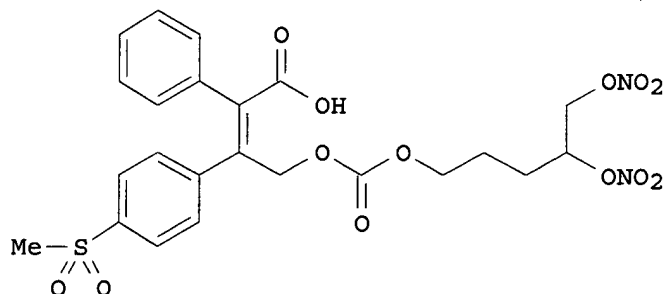
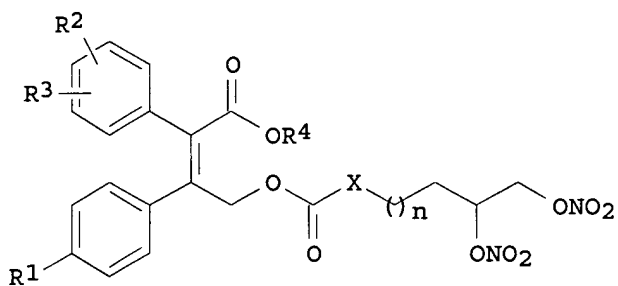
L4 22 SEA FILE=REGISTRY SSS FUL L1 OR L2

L5 2 SEA FILE=CAPLUS ABB=ON PLU=ON L4

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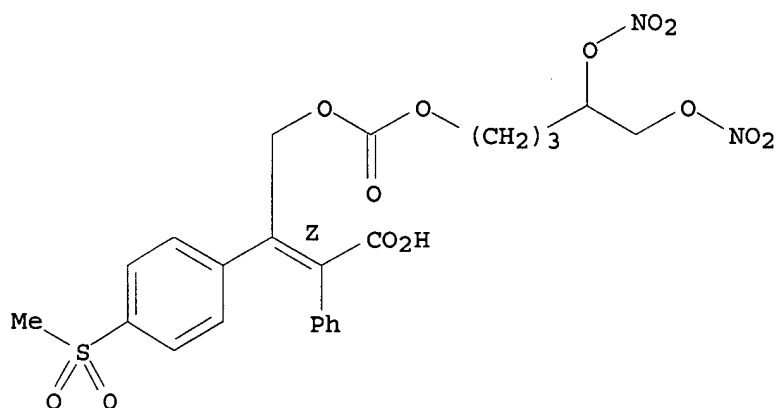
L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:696873 CAPLUS
 DN 143:172624
 TI Preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones
 as cyclooxygenase-2 inhibitors
 IN Dufresne, Claude; Berthelette, Carl; Li, Lianhai; Guay, Daniel; Gallant,
 Michel; Lacombe, Patrick; Aspiotis, Renee; Wang, Zhaoyin; Sturino, Claudio
 F.
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070883	A1	20050804	WO 2005-CA83	20050125
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	PRAI US 2004-539666P	P	20040127		
	OS MARPAT 143:172624				
	GI				



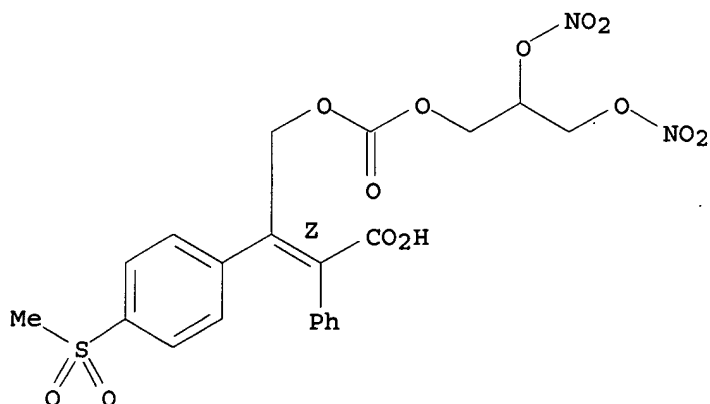
- AB Nitric oxide-releasing prodrugs I [X = O, CH₂; n = 1-6; R₁ = SO₂CH₃, SO₂NH₂; R₂-3 = H, halo, alkoxy, etc.; R₄ = H, alkyl, etc.] are prepared. For instance, II is prepared in several steps from 3,4-bis(nitrooxy)butyl alc., phosgene and (Z)-4-[(tert-butyldimethylsilyl)oxy]-2-[4-(methylsulfonyl)phenyl]-3-phenylbut-2-en-1-ol. I are useful for the treatment of cyclooxygenase-2 mediated diseases alone and in combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events [no data].
- IT 861430-32-2P 861430-35-5P
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors)
- RN 861430-32-2 CAPLUS
 CN Benzeneacetic acid, α-[2-[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



- RN 861430-35-5 CAPLUS
 CN Benzeneacetic acid, α-[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



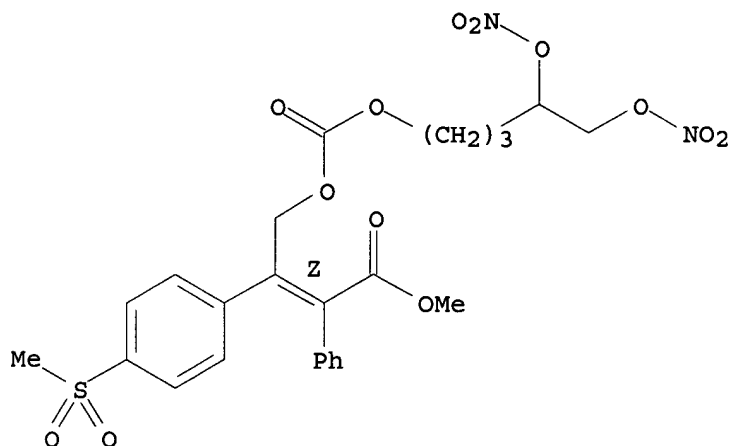
- IT 861430-33-3P 861430-34-4P 861430-36-6P
 861430-38-8P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors)

RN 861430-33-3 CAPLUS

CN Benzeneacetic acid, α -[2-[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, methyl ester, (α Z)-(9CI) (CA INDEX NAME)

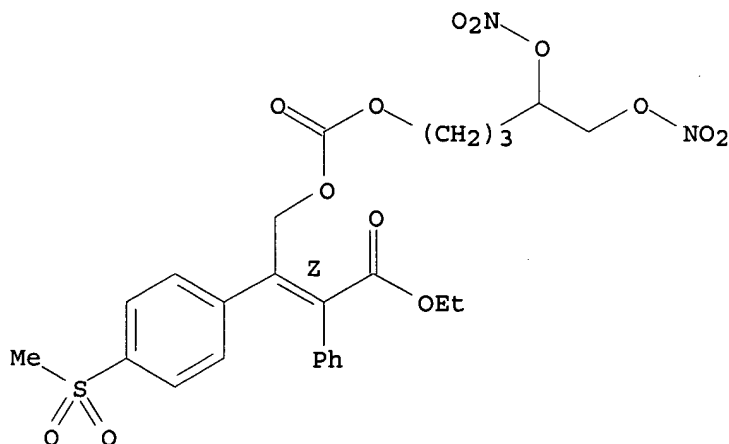
Double bond geometry as shown.



RN 861430-34-4 CAPLUS

CN Benzeneacetic acid, α -[2-[[[4,5-bis(nitrooxy)pentyl]oxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, ethyl ester, (α Z)-(9CI) (CA INDEX NAME)

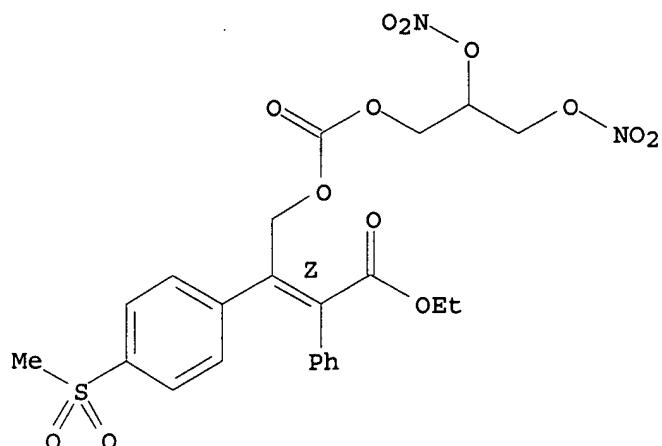
Double bond geometry as shown.



RN 861430-36-6 CAPLUS

CN Benzeneacetic acid, α -[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, ethyl ester, (α Z)-(9CI) (CA INDEX NAME)

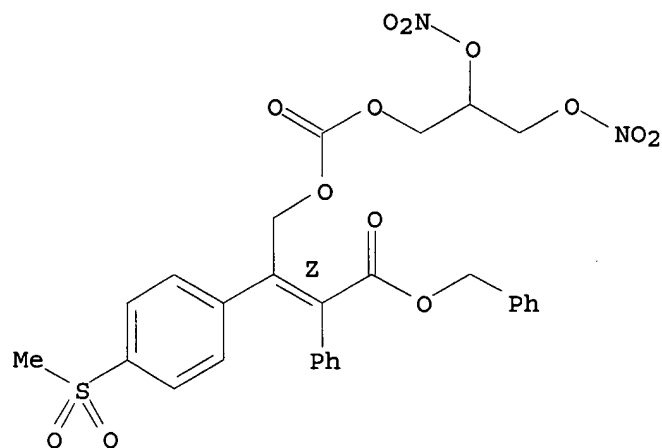
Double bond geometry as shown.



RN 861430-38-8 CAPLUS

CN Benzeneacetic acid, α -[2-[[[2,3-bis(nitrooxy)propoxy]carbonyl]oxy]-1-[4-(methylsulfonyl)phenyl]ethylidene]-, phenylmethyl ester, (α Z)- (9CI) (CA INDEX NAME)

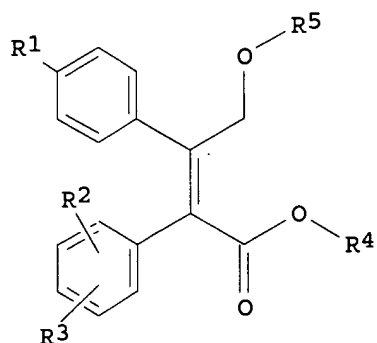
Double bond geometry as shown.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:101124 CAPLUS
 DN 140:163574
 TI Preparation of nitric oxide releasing diaryl-2-(5H)-furanone prodrugs as selective cyclooxygenase-2 inhibitors for treatment inflammatory diseases
 IN Berthelette, Carl; Lachance, Nicholas; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin; Young, Robert N.; Dufresne, Claude
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 129 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004011421	A1	20040205	WO 2003-CA1115	20030724
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	CA 2493082	AA	20040205	CA 2003-2493082	20030724
	AU 2003252515	A1	20040216	AU 2003-252515	20030724
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	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005261245	A1	20051124	US 2005-521075	20050112
PRAI	US 2002-398683P	P	20020726		
	US 2002-435341P	P	20021220		
	WO 2003-CA1115	W	20030724		
OS	MARPAT 140:163574				
GI					



I

AB Title compds. I [R1 = S(O)2CH3, S(O)2NH2, S(O)2NHC(=O)CF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = H, (un)substituted alkyl, e.g., halo, Ph, naphthyl, etc.; R5 = NOx, C(=O)-E-alkyl-W-NOx, C(=O)-E-alkyl-Ar-alkyl-W-NOx; x = 1, 2; E = bond, O, S, etc.; W = O, S, C[CO2Rb]2; Ar = (un)substituted Ph, naphthyl, HET3; HET3 = benzimidazolyl, benzofuranyl, benzopyrazolyl, etc.; Rb = (un)substituted alkyl, Ph, naphthyl, etc.] and their pharmaceutically acceptable salts were prepared For example, allylic bromination of Me (2E)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate, e.g., prepared from 1-(4-methanesulfonylphenyl)ethanone in 2 steps, followed

by O-alkylation of AgNO₃ afforded nitrate ester I [R₁ = 4-S(O)₂CH₃; R₂, R₃ = H; R₄ = CH₃; R₅ = NO₂] in 23% overall yield. In human whole blood LPS induced PGE₂ and TXB₂ production assays, compds. I have a COX-2 potency and COX-2/COX-1 selectivity comparable to rofecoxib. In paw edema assays in rat, compound I [R₁ = 4-S(O)₂CH₃; R₂, R₃ = H; R₄ = CH₃; R₅ = CO₂(CH₂)₄NO₂] exhibited 42-79% inhibition of pain at 1-30 mg/kg dosage. Of note, compds. I are prodrugs of rofecoxib analogs and are claimed useful for the treatment of chronic COX-2 mediated diseases, while reducing the risk of thrombotic cardiovascular events. Compds. I are useful for treatments of osteoarthritis, rheumatoid arthritis, and chronic pain.

IT 654069-13-3P

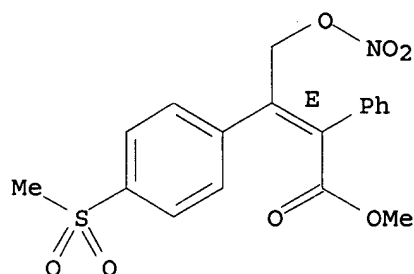
RL: BYP (Byproduct); PREP (Preparation)

(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)

RN 654069-13-3 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-(nitrooxy)ethylidene]-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 654068-74-3P 654068-76-5P 654068-77-6P

654068-79-8P 654068-81-2P 654068-82-3P

654068-83-4P 654068-84-5P 654068-85-6P

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654068-89-0P

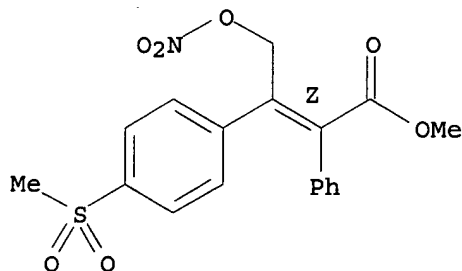
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)

RN 654068-74-3 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-(nitrooxy)ethylidene]-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

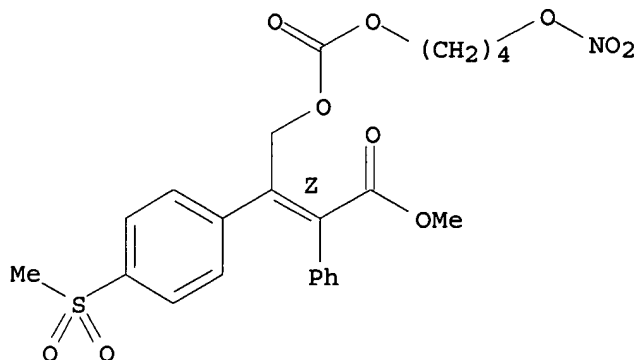


RN 654068-76-5 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[4-

(nitrooxy)butoxy]carbonyl]oxy]ethylidene]-, methyl ester, (α Z)-
(9CI) (CA INDEX NAME)

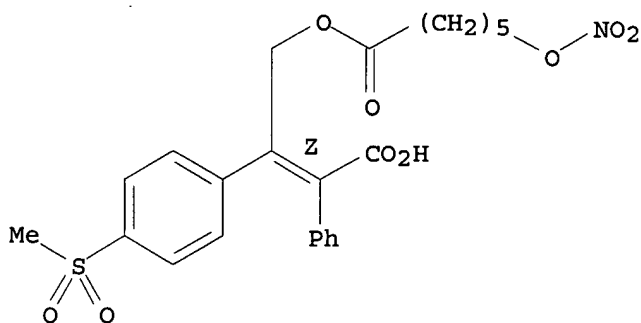
Double bond geometry as shown.



RN 654068-77-6 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (α Z)- (9CI) (CA INDEX NAME)

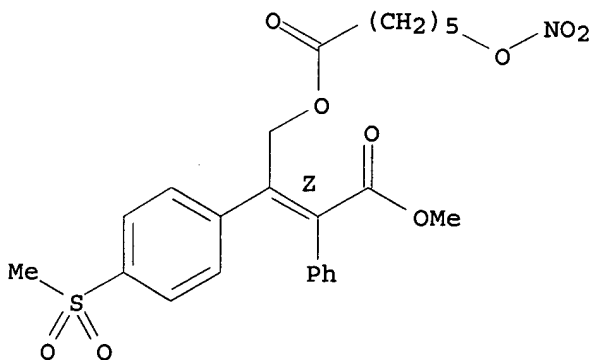
Double bond geometry as shown.



RN 654068-79-8 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, methyl ester, (α Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

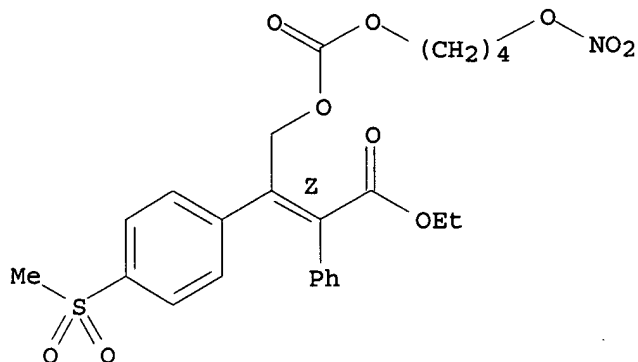


RN 654068-81-2 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[[4-(nitrooxy)butoxy]carbonyl]oxy]ethylidene]-, methyl ester, (α Z)- (9CI) (CA INDEX NAME)

(nitrooxy)butoxy]carbonyl]oxy]ethylidene]-, ethyl ester, (α Z)- (9CI)
(CA INDEX NAME)

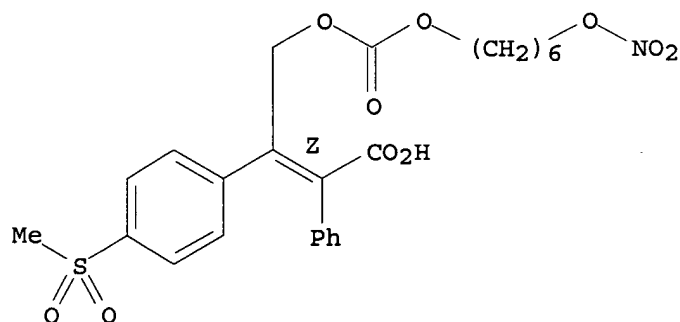
Double bond geometry as shown.



RN 654068-82-3 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, (α Z)- (9CI) (CA INDEX NAME)

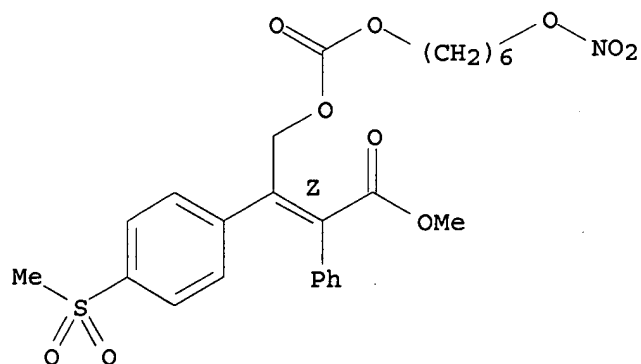
Double bond geometry as shown.



RN 654068-83-4 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, methyl ester, (α Z)- (9CI) (CA INDEX NAME)

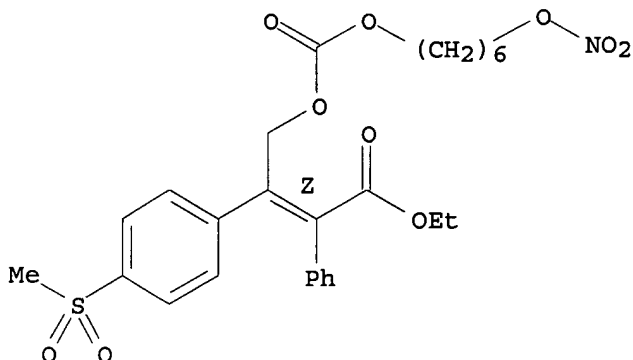
Double bond geometry as shown.



RN 654068-84-5 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[[6-(nitrooxy)hexyl]oxy]carbonyl]oxy]ethylidene]-, ethyl ester, (α Z)-(9CI) (CA INDEX NAME)

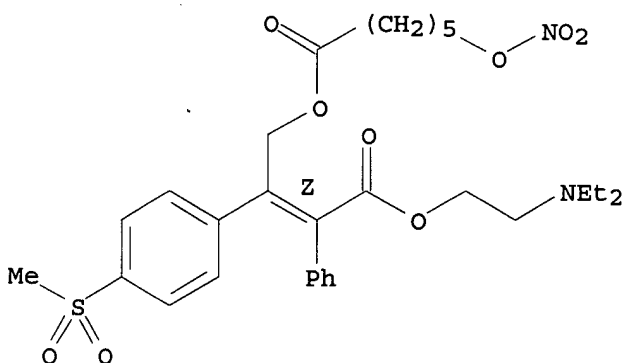
Double bond geometry as shown.



RN 654068-85-6 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, 2-(diethylamino)ethyl ester, (α Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

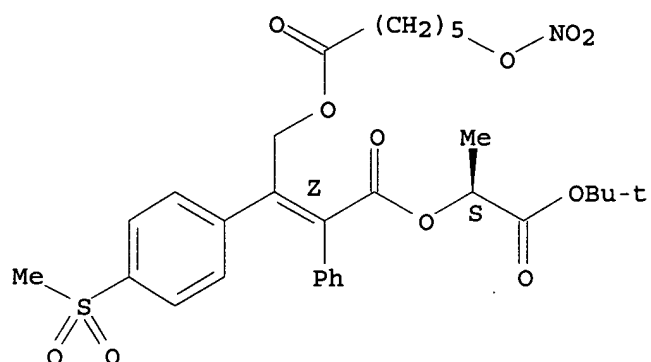


RN 654068-86-7 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (1S)-2-(1,1-dimethylethoxy)-1-methyl-2-oxoethyl ester, (α Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

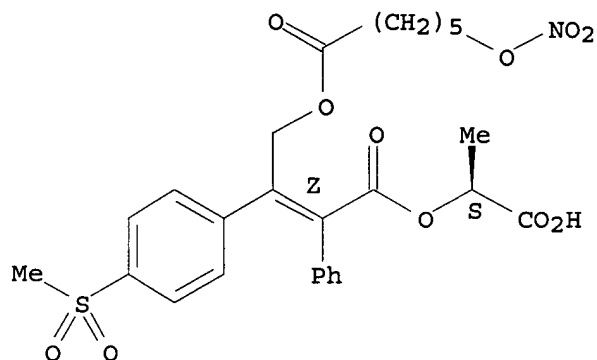
Double bond geometry as shown.



RN 654068-87-8 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[6-(nitrooxy)-1-oxohexyl]oxy]ethylidene]-, (1S)-1-carboxyethyl ester, (αZ)-(9CI)
(CA INDEX NAME)

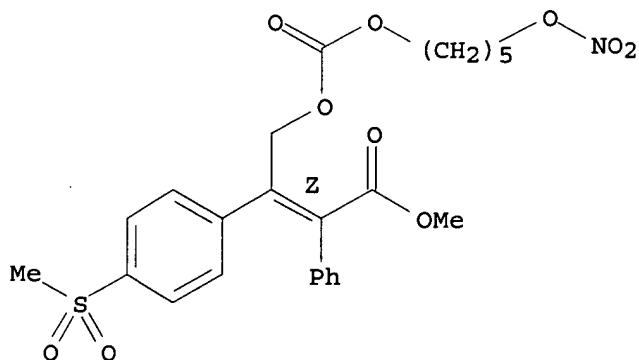
Absolute stereochemistry.
Double bond geometry as shown.



RN 654068-88-9 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[5-(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, methyl ester, (αZ)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

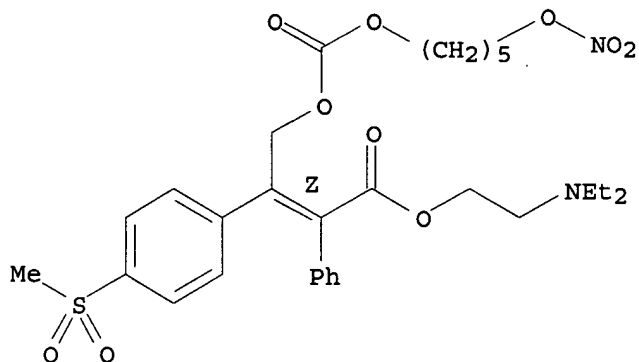


RN 654068-89-0 CAPLUS

CN Benzeneacetic acid, α-[1-[4-(methylsulfonyl)phenyl]-2-[[[5-

(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, 2-(diethylamino)ethyl ester, monohydrochloride, (α Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

IT 654069-07-5P

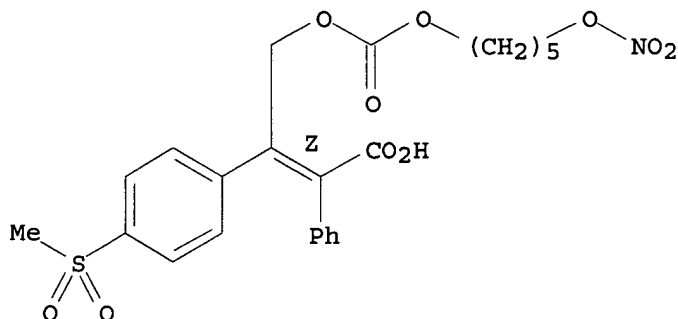
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of nitric oxide releasing diarylfuranone prodrugs as selective cyclooxygenase-2 inhibitors for treatment of inflammatory diseases)

RN 654069-07-5 CAPLUS

CN Benzeneacetic acid, α -[1-[4-(methylsulfonyl)phenyl]-2-[[[5-(nitrooxy)pentyl]oxy]carbonyl]oxy]ethylidene]-, (α Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

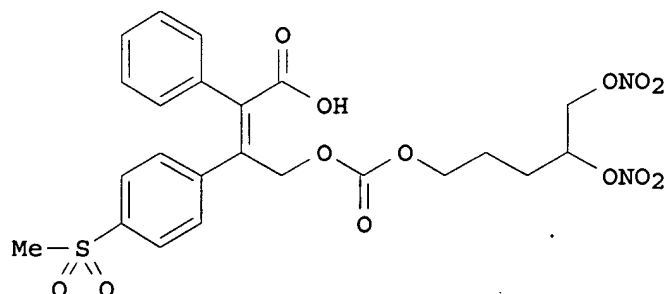
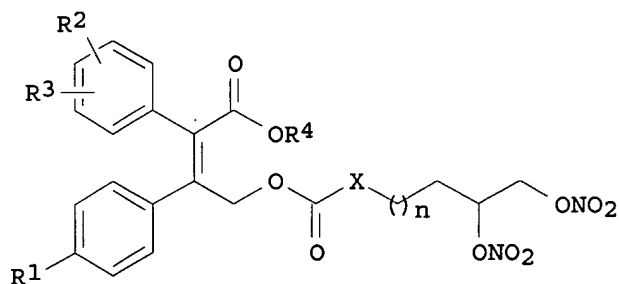
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L8	22	SEA FILE=CAPLUS ABB=ON	PLU=ON	"LI LIANHAI"/AU
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=> d 1-6 bib abs

L14 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:696873 CAPLUS
 DN 143:172624
 TI Preparation of nitric oxide releasing prodrugs
 of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors
 IN Dufresne, Claude; Berthelette, Carl; Li,
 Lianhai; Guay, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis,
 Renee; Wang, Zhaoyin; Sturino, Claudio F.
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070883	A1	20050804	WO 2005-CA83	20050125
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PRAI	US 2004-539666P	P	20040127		
OS	MARPAT 143:172624				
GI					



AB Nitric oxide-releasing prodrugs I [X = O, CH₂; n = 1-6; R₁ = SO₂CH₃, SO₂NH₂; R₂₋₃ = H, halo, alkoxy, etc.; R₄ = H, alkyl, etc.] are prepared For instance, II is prepared in several steps from 3,4-bis(nitrooxy)butyl alc., phosgene and (Z)-4-[(tert-butyl dimethylsilyl)oxy]-2-[4-(methylsulfonyl)phenyl]-3-phenylbut-2-en-1-ol. I are useful for the treatment of cyclooxygenase-2 mediated diseases alone and in combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events [no data].

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:696865 CAPLUS
 DN 143:193802
 TI Preparation of nitric oxide releasing prodrugs
 of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors
 IN Berthelette, Carl; Li, Lianhai; Beaulieu, Christian;
 Wang, Zhaoyin; Sturino, Claudio F.
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070874	A1	20050804	WO 2005-CA84	20050125
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 2004-540101P	P	20040127		
OS	MARPAT 143:193802				
GI					

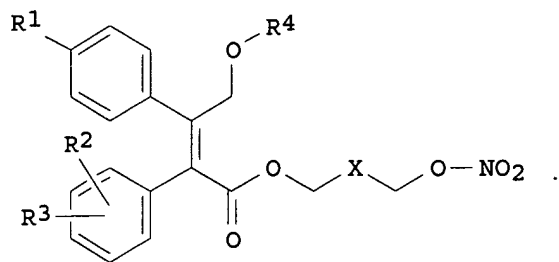
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [n = 1-6; R1 = SO₂CH₃, SO₂NH₂; R2-3 = H, halo, alkoxy, etc.; R4 = alkyl, Ph, etc.] are prepared For instance, II is prepared in several steps from 4-(4-(methanesulfonyl)phenyl)-3-phenyl-5H-furan-2-one and hex-5-en-1-ol. I are nitric oxide-releasing prodrugs of diaryl-2(5H)-furanones useful in the treatment of cyclooxygenase-2 mediated diseases [no data]. I may also be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events.

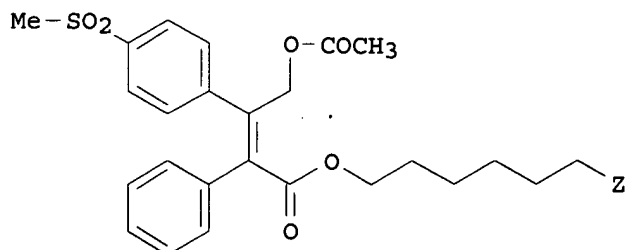
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:739958 CAPLUS
 DN 141:260542
 TI Preparation of nitric oxide releasing prodrugs
 of diaryl-2-(5H)-furanones as selective cyclooxygenase-2 inhibitors
 IN Berthelette, Carl; Li, Lianhai; Sturino,
 Claudio; Wang, Zhaoyin
 PA Can.
 SO U.S. Pat. Appl. Publ., 19 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004176331	A1	20040909	US 2004-790288	20040301
	AU 2004240700	A1	20041202	AU 2004-240700	20040301
	CA 2517490	AA	20041202	CA 2004-2517490	20040301
	WO 2004103955	A1	20041202	WO 2004-CA314	20040301
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1601644	A1	20051207	EP 2004-761562	20040301
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI	US 2003-452124P	P	20030305		
	WO 2004-CA314	W	20040301		
OS	MARPAT 141:260542				
GI					



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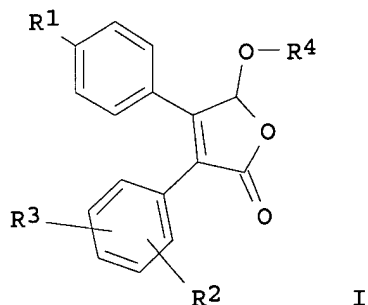


II

AB Title compds. I [$X = (CH_2)_n$; $n = 3-6$; $R_1 = SO_2Me, SO_2NH_2, SO_2NHCOCF_3$, etc.; $R_2, R_3 = H, \text{halo}, \text{alkoxy}, \text{etc.}$; $R_4 = CO\text{-alkyl}, CO(CH_2)_mNR_5R_6$; $m = 1-4$; $R_5, R_6 = H, \text{halo-substituted alkyl}$] and their pharmaceutically acceptable salts were prepared. For example, O-alkylation of $AgNO_3$ by bromide II ($Z = Br$), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II ($Z = -ONO_2$). In human blood PGE₂ inhibition production assays, nitrooxyhexyl II ($Z = -ONO_2$) exhibited an IC₅₀ value of 0.22 μM . Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions.

L14 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:412933 CAPLUS
 DN 140:423574
 TI Preparation of nitric oxide releasing prodrugs
 of diaryl-2-(5H)-furanones as cyclooxygenase-2 inhibitors
 IN Young, Robert N.; Wang, Zhaoyin
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

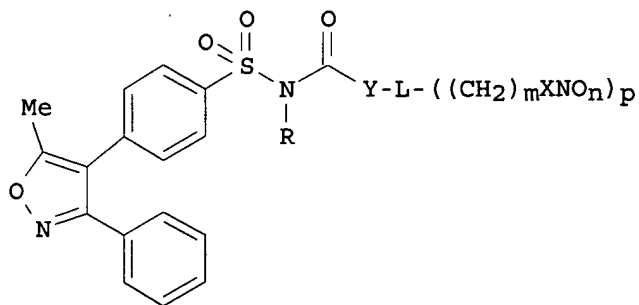
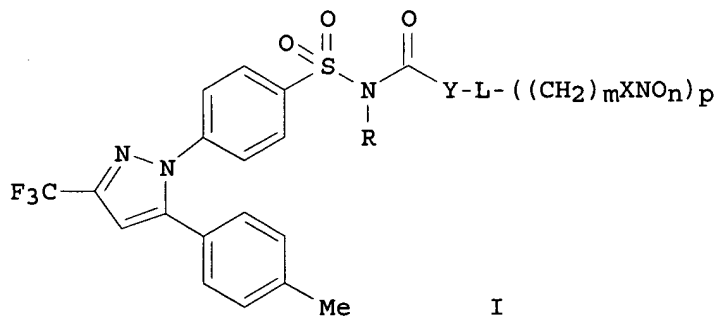
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041803	A1	20040521	WO 2003-CA1691	20031103
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	AU 2003283096	A1	20040607	AU 2003-283096	20031103
PRAI	US 2002-423866P	P	20021105		
	WO 2003-CA1691	W	20031103		
OS	MARPAT 140:423574				
GI					



AB The title compds. I [R1 = SO2Me, etc.; R2, R3 = H, halo, etc.; R4 = NOm, etc.; m = 1 or 2] are prepared The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases while simultaneously reducing the risk of thrombotic cardiovascular events.

L14 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:370913 CAPLUS
 DN 140:375166
 TI Preparation of nitric oxide releasing selective cyclooxygenase-2
 inhibitors
 IN Wang, Zhaoyin; Young, Robert N.; Zamboni, Robert
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

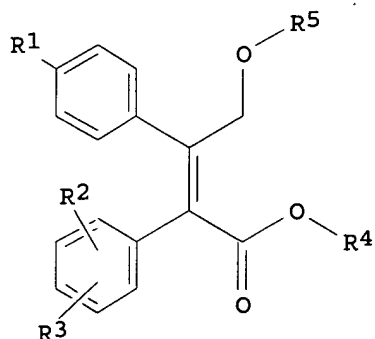
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004037798	A1	20040506	WO 2003-CA1605	20031021
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2503063	AA	20040506	CA 2003-2503063	20031021
	AU 2003278039	A1	20040513	AU 2003-278039	20031021
	EP 1562914	A1	20050817	EP 2003-769122	20031021
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006058363	A1	20060316	US 2005-530214	20050404
PRAI	US 2002-420292P	P	20021022		
	WO 2003-CA1605	W	20031021		
OS	MARPAT 140:375166				
GI					



AB Novel compds. of formulas I and II [R = H, alkyl; L = bond, alkylidene, cycloalkylidene, aryl, etc.; X = O, S; Y = bond, S, O, (substituted) NH; m = 0-4; n = 1-2; p = 1-4] are prepared, which are nitric oxide-releasing prodrugs useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compns. and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compds. I or II. The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while simultaneously reducing the risk of thrombotic cardiovascular events.

L14 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:101124 CAPLUS
 DN 140:163574
 TI Preparation of nitric oxide releasing
 diaryl-2-(5H)-furanone prodrugs as selective cyclooxygenase-2
 inhibitors for treatment inflammatory diseases
 IN Berthelette, Carl; Lachance, Nicholas; Li,
 Lianhai; Sturino, Claudio; Wang, Zhaoyin;
 Young, Robert N.; Dufresne, Claude
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 129 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004011421	A1	20040205	WO 2003-CA1115	20030724
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2493082	AA	20040205	CA 2003-2493082	20030724
	AU 2003252515	A1	20040216	AU 2003-252515	20030724
	EP 1527045	A1	20050504	EP 2003-771010	20030724
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2005261245	A1	20051124	US 2005-521075	20050112
PRAI	US 2002-398683P	P	20020726		
	US 2002-435341P	P	20021220		
	WO 2003-CA1115	W	20030724		
OS	MARPAT 140:163574				
GI					



AB Title compds. I [R1 = S(O)2CH3, S(O)2NH2, S(O)2NHC(=O)CF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = H, (un)substituted alkyl, e.g., halo, Ph, naphthyl, etc.; R5 = NOx, C(=O)-E-alkyl-W-NOx, C(=O)-E-alkyl-Ar-alkyl-W-NOx; x = 1, 2; E = bond, O, S, etc.; W = O, S, C[CO2Rb]2; Ar = (un)substituted Ph, naphthyl, HET3; HET3 = benzimidazolyl, benzofuranyl, benzopyrazolyl, etc.; Rb = (un)substituted alkyl, Ph, naphthyl, etc.] and their pharmaceutically acceptable salts were prepared For example, allylic

bromination of Me (2E)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate, e.g., prepared from 1-(4-methanesulfonylphenyl)ethanone in 2 steps, followed by O-alkylation of AgNO₃ afforded nitrate ester I [R1 = 4-S(O)₂CH₃; R2, R3 = H; R4 = CH₃; R5 = NO₂] in 23% overall yield. In human whole blood LPS induced PGE₂ and TXB₂ production assays, compds. I have a COX-2 potency and COX-2/COX-1 selectivity comparable to rofecoxib. In paw edema assays in rat, compound I [R1 = 4-S(O)₂CH₃; R2, R3 = H; R4 = CH₃; R5 = CO₂(CH₂)₄ONO₂] exhibited 42-79% inhibition of pain at 1-30 mg/kg dosage. Of note, compds. I are prodrugs of rofecoxib analogs and are claimed useful for the treatment of chronic COX-2 mediated diseases, while reducing the risk of thrombotic cardiovascular events. Compds. I are useful for treatments of osteoarthritis, rheumatoid arthritis, and chronic pain.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his full

(FILE 'HOME' ENTERED AT 12:23:14 ON 14 AUG 2006)

FILE 'REGISTRY' ENTERED AT 12:23:28 ON 14 AUG 2006

L1 STRUCTURE UPLOADED

D

L2 STRUCTURE UPLOADED

D

L3 1 SEA SSS SAM L1 OR L2

D SCAN

L4 22 SEA SSS FUL L1 OR L2

FILE 'CAPLUS' ENTERED AT 12:24:52 ON 14 AUG 2006

L5 2 SEA ABB=ON PLU=ON L4

D QUE L5 STAT

D 1-2 BIB ABS HITSTR

E BERTHELETTE CARL/AU

L6 26 SEA ABB=ON PLU=ON "BERTHELETTE C"/AU OR "BERTHELETTE CARL"/AU

E LACHANCE NICHOLAS/AU

L7 4 SEA ABB=ON PLU=ON "LACHANCE NICHOLAS"/AU

E LI LIANHAI/AU

L8 22 SEA ABB=ON PLU=ON "LI LIANHAI"/AU

E STURINO CLAUDIO/AU

L9 34 SEA ABB=ON PLU=ON ("STURINO C F"/AU OR "STURINO CLAUDIO"/AU OR "STURINO CLAUDIO F"/AU)

E WANG ZHAOYIN/AU

L10 72 SEA ABB=ON PLU=ON "WANG ZHAOYIN"/AU

E YOUNG ROBERT/AU

E YOUNG ROBERT N/AU

L11 130 SEA ABB=ON PLU=ON ("YOUNG ROBERT N"/AU OR "YOUNG ROBERT NORMAN"/AU)

E DUFRESNE CLAUDE/AU

L12 104 SEA ABB=ON PLU=ON "DUFRESNE CLAUDE"/AU

L13 339 SEA ABB=ON PLU=ON L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12

L14 6 SEA ABB=ON PLU=ON L13 AND ((NITRIC (W) OXIDE) (L) PRODRUG)

D QUE L14 STAT

D 1-6 BIB ABS

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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DICTIONARY FILE UPDATES: 13 AUG 2006 HIGHEST RN 901009-82-3

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